Neurobiology of Sleep and Circadian Rhythms 5 (2018) 84–93

Contents lists available at ScienceDirect

Neurobiology of Sleep and Circadian Rhythms

journal homepage: www.elsevier.com/locate/nbscr

Research paper

Dose response of acute cocaine on sleep/waking behavior in mice

Theresa E. Bjorness[a,b,*], Robert W. Greene[b,c,d,e]

[a] Research Service, VA North Texas Health Care System, 4500 S. Lancaster Dr., Dallas, TX 75216, United States
[b] Department of Psychiatry, University of Texas Southwestern, Dallas, TX 75390, United States
[c] Department of Neuroscience, University of Texas Southwestern, Dallas, TX 75390, United States
[d] Mental Health Service, VA North Texas Health Care System, Dallas, TX, 75216, United States
[e] International Institute for Integrative Sleep Medicine, University of Tsukuba, Tsukuba, Japan 305-8577

ARTICLE INFO

Keywords:
Insomnia
Addiction
Substance use disorder
Homeostatic sleep need

ABSTRACT

Chronic cocaine use has been associated with sleep disturbances, both during active use periods and during withdrawal and abstinence. Acute cocaine also increases waking at the expense of slow wave sleep and Rapid Eye Movement in non-human subjects. However, the effects of acute cocaine on sleep/waking activity in mice, a rodent model commonly used in both sleep and addiction research due to its high genetic tractability, has yet to be investigated. Sleep/waking activity was measured via polysomnography following IP administration of three doses of cocaine (3.6, 9.6, 18 mg/kg) and vehicle control in male C57BL/6 mice. Cocaine dose-dependently increased sleep latency, increased waking time and increased fast EEG activity within waking. Increases in waking occurred primarily during the first hour following injection, followed by rebound SWS sleep. Sleep/waking activity normalized within a 24-hour period. As with humans and other rodents, cocaine dose dependently reduces sleep in a wildtype strain of mice commonly used in reward and addiction research.

1. Introduction

Cocaine is a psychomotor stimulant which induces arousal and locomotor activity/hyperactivity following administration. As a drug with high abuse potential, there has been a substantial amount of research, both in human users and in preclinical models, into the consequences of cocaine use and potential therapeutic avenues (for review, Johanson and Fischman, 1989; Hanlon et al., 2013; Czoty et al., 2016), including research into sleep behavior. Sleep disruption has been observed under both binge taking and abstinence conditions in humans (Coffey et al., 2000; Pace-Schott et al., 2005; Angarita et al., 2016). In addition to changes in overall sleep time, during abstinence cocaine use has been reported to increase stage 2 slow wave sleep (SWS) at the expense of stage 3 and 4 SWS (Irwin et al., 2016), decrease Rapid Eye Movement (REM) latency (Johanson et al., 1999; Pace-Schott et al., 2005; Irwin et al., 2016), and increase REM time (Valladares and Irwin, 2007; Irwin et al., 2016).

Similar to the effects of binge cocaine and abstinence in humans, cocaine reduces sleep/waking activity in rats (Dugovic et al., 1992; Knapp et al., 2007; Chen et al., 2015) with some rebound sleep following acute administration (Dugovic et al., 1992; Knapp et al., 2007). However, the effect of acute or sub chronic cocaine on sleep/waking behavior in mice, a species often used in addiction and behavior research due to relative ease of genetic manipulations, has not been measured. Here, we show that cocaine dose-dependently increases sleep latency and REM latency, increases waking time by increasing the duration of waking episodes, alters EEG spectral density and induces a sleep rebound response.

2. Materials and methods

2.1. Animals

Adult male C57BL/6 mice (n = 7) were single housed following implantation of electrodes in a 12:12 light/dark cycle with food and water available ad libitum. All experiments were approved by the VA North Texas Health Care System IACUC. All efforts were made to minimize animal suffering and to reduce the number of animals used.

2.2. Surgical procedures

EEG and EMG electrodes were implanted as previously described (Bjorness et al., 2016). Briefly, mice were anesthetized with isoflurane and placed into a stereotaxic frame. Holes were drilled over the frontal cortex, over the right parietal cortex, and over the left occipital cortex after which custom EEG electrodes (Plastics One electrodes, Small Parts

* Corresponding author at: Research Service, VA North Texas Health Care System, 4500 S. Lancaster Dr., Dallas, TX 75216, United States.
E-mail address: theresa.bjorness@utsouthwestern.edu (T.E. Bjorness).

https://doi.org/10.1016/j.nbscr.2018.02.001
Received 6 November 2017; Received in revised form 7 February 2018; Accepted 22 February 2018
Available online 24 February 2018
2451-9944/ Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/BY-NC-ND/4.0/).

screws) were threaded into the holes. EMG electrodes (Plastics One) were placed under the dorsal nuchal muscle, the EEG and EMG electrodes were gathered into a six hole pedestal (Plastics One), and affixed to the skull via dental cement. The implant was coated with triple antibiotic ointment and the mice were given one administration of 0.03 mg buprenorphine for pain relief. Mice were given two weeks to recover from surgical procedures prior to acclimation to recording tethers.

2.3. Polysomnography and experimental design

Following recovery from implantation of electrodes, mice were habituated to recording tethers as previously described (Bjorness et al., 2016). Mice were housed in cages set above a treadmill belt throughout the recording period with a room temperature of 22.0 + /-1 ∘C. First, baseline, undisturbed EEG/EMG activity was measured for one day, after which mice were given saline, 3.6 mg/kg cocaine, 9.6 mg/kg cocaine, and 18 mg/kg cocaine with one injection (IP) per day on successive days. Injections were administered between zeitgeber time (ZT) 4.5–5.5 (i.e. 4.5–5.5 h following the start of the light period); this period was chosen since most behavioral testing in rodents occurs during the light phase, including addiction-related reward testing such as conditioned place preference and locomotor sensitization and occurs following the peak of SWS SWA early in the light phase (Bjorness et al., 2016). Saline was always the first injection to provide the experience of being removed from the cage while connected to the recording tether and injected, while 18 mg/kg cocaine was always the final injection (order of 3.6 mg/kg and 9.6 mg/kg cocaine counterbalanced between two sets of mice, first set n = 4, second set n = 3) since this dose carried the highest risk of inducing sensitization such that subsequent cocaine exposures would be followed by greater locomotor activity or stereotypy. These doses were chosen to represent low (subthreshold for conditioned place preference with this strain, Zachariou et al., 2001) moderate (typically induces conditioned place preference), and high (induces locomotor sensitization with this strain, Mongi-Bragato et al., 2016). Signals were scored offline using a custom Matlab (Mathworks) sleepscorer program by a scorer blinded to the condition (baseline/saline/cocaine) and epochs containing artifact were flagged and removed from power analysis. Waking, SWS, and REM sleep were defined using standard criteria as described previously (Bjorness et al., 2009; Bjorness et al., 2016), while power spectrum values were calculated as described previously (Bjorness et al., 2016).

2.4. Outcome measures

Three sets of outcome measures were used. First, objective measures of sleep time were calculated, including: latency to enter SWS, latency to enter prolonged SWS, latency to enter REM, percent time in state, average episode duration, and number of episodes. Episodes were defined as previously described (Bjorness et al., 2016). Briefly, an episode was initiated with three consecutive 10 second epochs of the same state and ended by three consecutive 10 second epochs of a different state. Second, homeostatic sleep drive, the increased drive in sleep that builds progressively during waking (Borbely, 1982), was assessed via slow wave activity (SWA, 0.5–4.5 Hz) normalized to average 24 h gamma (30–50 Hz, as described previously, Bjorness et al., 2016). Third, changes in spectral density were calculated using relative SWA, theta (6–10 Hz), spindle (8–16 Hz), sigma (16–30 Hz), and gamma normalized to total EEG power and compared to power at the same circadian time during baseline (percent change from baseline). These values were calculated in 1 h bins with the exception of relative band power across 24 h which was averaged across the entire 24 h period.

2.5. Drugs

Cocaine hydrochloride (Sigma Aldrich) was dissolved in sterile saline. Buprenoprhine (VANTXHS Pharmacy) was diluted in sterile saline.

3. Statistical analysis

For all outcome measures except sleep latency and spectral power, values were compared in three time frames; first, values within the first hour following injection were compared using a one-way ANOVA with repeated measures, second, values within the first 6 h following injection were compared using a two-way ANOVA with repeated measures (condition x time), and third, percent change from baseline across 24 h was calculated in 2 (waking and SWS) or 4 (REM) hour bins and compared via one way ANOVA with repeated measures. Longer bins were necessary for REM sleep averages since some animals did not show REM sleep for prolonged periods following injection. For sleep latency measures, one-way ANOVAs were used to compare latency to enter sleep (defined as the first episode of sleep with a minimum duration of 30 s), latency to enter prolonged SWS (defined as the first episode of SWS with a minimum duration of 5 min), and latency to enter REM sleep (defined as the first episode of REM sleep with a minimum duration of 30 s) following cocaine injection to sleep latency following saline injection. A one way ANOVA with repeated measures was used to compare the change in relative band power from baseline between injection conditions. A one sample t test was used to compare change in relative band power to baseline using a hypothetical value of 0. GraphPad Prism (GraphPad) was used for statistical analysis with statistical significance set at $p < 0.05$. One animal was excluded due to a bad injection for the 9.6 mg/kg dose. Exclusion was necessary for all analyses due to the use of repeated measures. Statistical comparisons and significance levels for each outcome measure is provided in the Supporting Information.

4. Results

4.1. Cocaine dose dependently increased sleep latency

Compared with saline injection, cocaine increased the latency to enter sleep (Fig. 1a, $F(2.148,10.74) = 18.66$, $p = 0.0003$) by 16.4 to 55.3 min (lowest and highest doses, respectively), to enter prolonged SWS (as defined as an episode of at least 5 min in duration (Fig. 1b, $F(1.612,8.058) = 33.64$, $p = 0.0002$)), and to enter REM sleep (Fig. 1c, $F(1.438,7.191) = 38.86$, $p = 0.0002$). Furthermore, there was a significant increase in latency to enter sleep, to enter prolonged sleep, and to enter REM between the lowest (3.6 mg/kg) and highest (18 mg/kg) doses of cocaine with additional differences between the middle (9.6 mg/kg) and highest dose of cocaine for the latency to enter sleep and enter prolonged SWS but not to enter REM sleep.

4.2. Increases in waking time occur primarily within the first 2 h post injection

Injection of saline or any of the three doses of cocaine increased time in waking ($F(1.682,8.409) = 48.11$, $p = 0.001$) and decreased time in SWS and REM in the first hour post injection compared to undisturbed baseline conditions (Fig. 2a, $F(1.576,7.878) = 39.93$, $p = 0.001$ and $F(1.582,7.909) = 16.88$, $p = 0.002$, respectively). Additionally, waking was increased and SWS decreased between saline and the highest dose of cocaine within this same period. Futhermore, increased waking between saline and the highest dose of cocaine was also apparent in the second hour following injection, while REM was decreased with all three cocaine doses in the second hour following injection compared to both baseline and saline conditions (Fig. 2b). When comparing waking/sleep time to change from baseline at the same circadian time, there was a significant effect of time ($F(11,55) = 3.993$, $p = 0.0003$), condition (substance/dose injected, $F(3,15) = 5.095$, $p = 0.0125$), and time x condition interaction for waking time (F

Download English Version:

https://daneshyari.com/en/article/8838698

Download Persian Version:

https://daneshyari.com/article/8838698

Daneshyari.com